



App. No. 09/269,321

Amendment dated February 13, 2004

Reply to Final Office Action of August 13, 2003

**Amendments to the Claims:**

This listing of claims will replace all prior versions, and listings, of claims in the application:

**Listing of Claims:**

1 – 14. (Canceled)

15. (Previously presented) The method of claim 25, wherein the nucleic acid cassette is present in a viral vector or nucleic acid delivery system.

16. (Previously presented) The method of claim 25 wherein the malignant cell is a solid tumor.

17. (Previously presented) The method of claim 16 wherein the solid tumor is a glioma.

18. (Original) The method of claim 17, wherein the nucleic acid cassettes is present in a vector, wherein the vector is an adenovirus vector or a herpes virus vector.

19. (Original) The method of claim 16, wherein the nucleic acid sequence of interest encodes a negative potentiator.

20. (Previously presented) The method of claim 19, wherein the gene of interest is a suicide gene, a dominant negative mutant or a cytotoxin.

21. (Previously presented) The method of claim 20, wherein the gene of interest is a suicide gene.

22. (Original) The method of claim 21, wherein the suicide gene is HSV thymidine kinase.

23. (Previously presented) The method of claim 20, wherein the gene of interest is a cytotoxin.

24. (Previously presented) The method of claim 23, wherein the cytotoxin contains at least Domain III of *Pseudomonas extoxin A*.

25. (Currently amended) A method of selectively expressing a gene in a malignant cell comprising:

(a) determining whether a the malignant cell expresses sufficient E2F to cause increased expression of a gene operably linked to an E2F responsive promoter when compared to a mitotically active non-malignant cell;

(b) adding an effective amount of a nucleic acid cassette to the malignant cell that was determined to express sufficient E2F, wherein said nucleic acid cassette comprises an E2F responsive promoter operably linked to a gene of interest, wherein said gene encodes a protein that stimulates production or expression of a cellular product, a positive potentiator or encodes a gene that inhibits production or expression of a cellular product, a negative potentiator;

(c) waiting until the nucleic acid cassette transduces the malignant cell; and

(d) selectively expressing the gene by the E2F in said malignant cell causing the E2F responsive promoter to express said gene.

26. (Previously presented) The method of claim 25, wherein the E2F responsive promoter is selected from the group of promoters consisting of E2F1 promoter, dihydrofolate reductase promoter, DNA polymerase  $\alpha$  promoter, c-myc promoter and  $\beta$ -myb promoter.

27. (Previously presented) The method of claim 25, wherein the gene of interest is selected from the group consisting of cytokines or costimulatory molecules.

28. (New) A method of selectively expressing a gene in a malignant cell relative to a non-malignant cell comprising:

(a) determining whether the malignant cell expresses sufficient E2F to activate an E2F responsive promoter to result in expression of higher levels of a gene operably linked to an E2F responsive promoter as compared to expression of the gene operably linked to a constitutive promoter;

(b) adding an effective amount of a nucleic acid cassette to the malignant cell that was determined to express sufficient E2F, wherein said nucleic acid cassette comprises an E2F responsive promoter operably linked to a gene of interest, wherein said gene encodes a protein that stimulates production or expression of a cellular product, a positive potentiator or encodes a gene that inhibits production or expression of a cellular product, a negative potentiator;

(c) waiting until the nucleic acid cassette transduces the malignant cell; and

(d) selectively expressing the gene by the E2F in said malignant cell causing the E2F responsive promoter to express said gene.

29. (New) The method of claim 28, wherein the nucleic acid cassette is present in a viral vector or nucleic acid delivery system.
30. (New) The method of claim 25, wherein the malignant cell is a solid tumor.
31. (New) The method of claim 30, wherein the solid tumor is a glioma.
32. (New) The method of claim 31, wherein the nucleic acid cassettes is present in a vector, wherein the vector is an adenovirus vector or a herpes virus vector.
33. (New) The method of claim 30, wherein the nucleic acid sequence of interest encodes a negative potentiator.
34. (New) The method of claim 33, wherein the gene of interest is a suicide gene, a dominant negative mutant or a cytotoxin.
35. (New) The method of claim 34, wherein the gene of interest is a suicide gene.
36. (New) The method of claim 35, wherein the suicide gene is HSV thymidine kinase.
37. (New) The method of claim 34, wherein the gene of interest is a cytotoxin.
38. (New) The method of claim 37, wherein the cytotoxin contains at least Domain III of *Pseudomonas extoxin A*.
39. (New) The method of claim 38, wherein the gene of interest is selected from the group consisting of cytokines or costimulatory molecules.

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40. (New) The method of claim 28, wherein the gene of interest is a marker gene.